

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 1196WOORD01	FOR FURTHER ACTION		See Form PCT/IPEA/416
International application No. PCT/EP2004/051120	International filing date (day/month/year) 15.06.2004	Priority date (day/month/year) 16.06.2003	
International Patent Classification (IPC) or national classification and IPC A61K31/495, A61K38/17, A61P11/00, A61K45/06			
Applicant ALTANA PHARMA AG et al.			
<ol style="list-style-type: none"> 1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36. 2. This REPORT consists of a total of 6 sheets, including this cover sheet. 3. This report is also accompanied by ANNEXES, comprising: <ol style="list-style-type: none"> a. <input type="checkbox"/> sent to the applicant and to the International Bureau) a total of sheets, as follows: <ul style="list-style-type: none"> <input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions). <input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box. b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions). 			
<ol style="list-style-type: none"> 4. This report contains indications relating to the following items: <ul style="list-style-type: none"> <input checked="" type="checkbox"/> Box No. I Basis of the opinion <input type="checkbox"/> Box No. II Priority <input checked="" type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability <input type="checkbox"/> Box No. IV Lack of unity of invention <input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement <input type="checkbox"/> Box No. VI Certain documents cited <input type="checkbox"/> Box No. VII Certain defects in the international application <input type="checkbox"/> Box No. VIII Certain observations on the international application 			
Date of submission of the demand 18.12.2004		Date of completion of this report 30.06.2005	
Name and mailing address of the International preliminary examining authority: <div style="display: flex; align-items: center;"> <div> European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465 </div> </div>		Authorized Officer Telephone No. +49 89 2399-	



INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY

30/560116

International application No.
PCT/EP2004/051120

IAP8 Rec'd PCT/TO 09 DEC 2005

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
 - ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
 - ☐ international search (under Rules 12.3 and 23.1(b))
 - ☐ publication of the international application (under Rule 12.4)
 - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages

1-20 as originally filed

Claims, Numbers

1-17 as originally filed

- ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing
3. ☐ The amendments have resulted in the cancellation of:
 - ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing *(specify)*:
 - ☐ any table(s) related to sequence listing *(specify)*:
 4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
 - ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing *(specify)*:
 - ☐ any table(s) related to sequence listing *(specify)*:

* If item 4 applies, some or all of these sheets may be marked "superseded."

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
- ☒ claims Nos. 1,3-15,26-28 in respect of industrial applicability

because:

- ☒ the said international application, or the said claims Nos. 1,3-15,26-28 in respect of industrial applicability relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the said claims Nos.
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
- | | |
|----------------------------|--|
| the written form | <input type="checkbox"/> has not been furnished |
| | <input type="checkbox"/> does not comply with the standard |
| the computer readable form | <input type="checkbox"/> has not been furnished |
| | <input type="checkbox"/> does not comply with the standard |
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.
- ☐ See separate sheet for further details

**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/EP2004/051120

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-17
	No: Claims	
Inventive step (IS)	Yes: Claims	
	No: Claims	1-17
Industrial applicability (IA)	Yes: Claims	2,16-25
	No: Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

IAPO 09 DEC 2005

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims 1, 3-15 and 26-28 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. The documents cited in the International Search Report (ISR) are consecutively numbered D1-D9 in the order of their listing. If not indicated otherwise, reference is made to the passages cited in said ISR.
2. The subject-matter of claims 1 to 28 appears to be novel in the sense of Article 33(2) PCT, since none of the documents of the search report disclose a combination of a PDE5 inhibitor and a pulmonary surfactant.
3. However, claims 1 to 28 cannot be considered as involving an inventive step, Art. 33(3) PCT for the following reasons:

The use of PDE5 inhibitors for the treatment of some pulmonary/lung diseases is known from D1-D5.

Pulmonary surfactants are also known to be useful in the treatment of pulmonary diseases (see D6-D9).

In the absence of appropriate evidence (e.g. experimental data) that specific combinations provide a synergistic effect in the treatment of a specific disease, an inventive step cannot be acknowledged and the invention claimed has to be regarded as arbitrary combinations of compounds.

The applicant is also reminded that synergistic effects are not predictable and are, per definition, unexpected. Thus, even if the applicant would show a synergistic

effect for a specific combination, this would not mean that the other possible claimed combinations would be considered as involving an inventive step, specially taking into account that the specific compounds are structurally different.

4. For the assessment of the present claims 1, 3-15 and 26-28 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 1196WOORD01	FOR FURTHER ACTION see Form PCT/ISA/220 as well as, where applicable, Item 5 below.	
International application No. PCT/EP2004/051120	International filing date (day/month/year) 15/06/2004	(Earliest) Priority Date (day/month/year) 16/06/2003
Applicant ALTANA PHARMA AG		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 04 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☐ Certain claims were found unsearchable (See Box II).

3. ☐ Unity of invention is lacking (see Box III).

4. With regard to the title,

☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows:

COMPOSITION COMPRISING A PULMONARY SURFACTANT AND A PDE5 INHIBITOR FOR THE TREATMENT OF LUNG DISEASES

5. With regard to the abstract,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regards to the drawings,

- a. the figure of the drawings to be published with the abstract is Figure No. _____

☐ as suggested by the applicant.

☐ as selected by this Authority, because the applicant failed to suggest a figure.

☐ as selected by this Authority, because this figure better characterizes the invention.

- b. ☐ none of the figures is to be published with the abstract.

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 A61K31/495 A61K38/17 A61P11/00 A61K45/06		
According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) IPC 7 A61K A61P		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practical, search terms used) EPO-Internal, WPI Data, PAJ, BIOSIS, EMBASE		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	EP 1 223 170 A (TAKEDA CHEMICAL INDUSTRIES, LTD. OSAKA-SHI, OSAKA 541-0045 (JP)) 17 July 2002 (2002-07-17) see claim 34; p.187, 1.10-16	1-28
Y	SUTTORP N ET AL: "PHOSPHODIESTERASEN-INHIBITION UND PULMONALE STROMBAHN - EIN NEUER THERAPIEANSATZ?" ATEMWEGS UND LUNGENKRANKHEITEN, DUSTRI-VERLAG, MUENCHEN-DEISENHOFEN, DE, vol. 22, no. 11, 1996, pages 560-566, XP002037141 table 3 <div style="text-align: center; margin-top: 10px;">----- -/--</div>	1-28
<div style="display: flex; justify-content: space-between;"> <input checked="" type="checkbox"/> Further documents are listed in the continuation of box C. <input checked="" type="checkbox"/> Patent family members are listed in annex. </div>		
<div style="display: flex;"> <div style="flex: 1;"> <p>* Special categories of cited documents:</p> <p>*A* document defining the general state of the art which is not considered to be of particular relevance</p> <p>*E* earlier document but published on or after the international filing date</p> <p>*L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</p> <p>*O* document referring to an oral disclosure, use, exhibition or other means</p> <p>*P* document published prior to the international filing date but later than the priority date claimed</p> </div> <div style="flex: 1;"> <p>*T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</p> <p>*X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone</p> <p>*Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.</p> <p>* & * document member of the same patent family</p> </div> </div>		
Date of the actual completion of the international search <div style="text-align: center; font-weight: bold; margin-top: 10px;">29 October 2004</div>		Date of mailing of the international search report <div style="text-align: center; font-weight: bold; margin-top: 10px;">09/11/2004</div>
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016		Authorized officer <div style="text-align: center; font-weight: bold; margin-top: 10px;">Pacreu Largo, M</div>

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	TWOHIG H J ET AL: "SILDENAFIL DECREASES ARTERIAL OXYGEN LEVELS IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE" THORAX, BMJ PUBLISHING GROUP, GB, vol. 55, no. SUPPL 3, 13 December 2000 (2000-12-13), page A40, XP001118097 ISSN: 0040-6376 abstract	1-28
Y	GHOFRANI H A ET AL: "Sildenafil for treatment of lung fibrosis and pulmonary hypertension: a randomised controlled trial" LANCET, XX, XX, vol. 360, no. 9337, 21 September 2002 (2002-09-21), pages 895-900, XP004381834 ISSN: 0140-6736 abstract	1-28
Y	ZHAO L ET AL: "SILDENAFIL INHIBITS HYPOXIA-INDUCED PULMONARY HYPERTENSION" CIRCULATION, AMERICAN HEART ASSOCIATION, DALLAS, TX, US, vol. 104, no. 4, 24 July 2001 (2001-07-24), pages 424-428, XP001162716 ISSN: 0009-7322 abstract	1-28
Y	WO 00/27360 A (BYK GULDEN LOMBERG CHEM FAB ;HAEFNER DIETRICH (DE)) 18 May 2000 (2000-05-18) claims	1-28
Y	WO 01/58423 A (BYK GULDEN LOMBERG CHEM FAB ;HAEFNER DIETRICH (DE)) 16 August 2001 (2001-08-16) claims	1-28
Y	LEWIS J F ET AL: "ROLE OF EXOGENOUS SURFACTANT IN ACUTE LUNG INJURY" CRITICAL CARE MEDICINE, WILLIAMS AND WILKINGS COMPANY, BALTIMORE, MA, US, vol. 31, no. 4, SUPPL, April 2003 (2003-04), pages S324-S328, XP009024097 ISSN: 0090-3493 the whole document	1-28
Y	WO 98/35683 A (BYK GULDEN LOMBERG CHEM FAB ;HAEFNER DIETRICH (DE)) 20 August 1998 (1998-08-20) cited in the application see claim 8; p.8, 1.4-11	1-28

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
EP 1223170	A	17-07-2002	AU 7683500 A	23-04-2001
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			JP 2003522138 T	22-07-2003
			US 2003091509 A1	15-05-2003
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			AU 734122 B2	07-06-2001
			AU 6497398 A	08-09-1998
			BR 9807399 A	14-03-2000
			CA 2276429 A1	20-08-1998
			CN 1123345 B	08-10-2003
			CZ 9902914 A3	16-02-2000
			EA 1758 B1	27-08-2001
			EE 9900279 A	15-02-2000
			WO 9835683 A1	20-08-1998
			EP 0977577 A1	09-02-2000
			HK 1026145 A1	02-07-2004
			JP 2001512452 T	21-08-2001
			NO 993875 A	11-08-1999
			NZ 336569 A	27-04-2001
			PL 335134 A1	10-04-2000
			TR 9901772 T2	21-09-1999
			US 2002132835 A1	19-09-2002
			US 6436970 B1	20-08-2002
			HU 0001043 A2	28-09-2000